ORIGINAL RESEARCH

Application of Magnetic Resonance T1rho and T2 Mapping in Evaluating Cartilage Injury in Middle-aged and Elderly Patients with Knee Osteoarthritis

Li Tang, MM; Yanfang Gao, BM; Chengzhe Deng, BM; Yurong Gong, BM

ABSTRACT

Objective • To investigate magnetic resonance longitudinal relaxation time quantitative imaging (T1rho) and transverse relaxation time quantitative imaging (T2 mapping) techniques in evaluating cartilage damage in middle-aged and elderly patients with knee osteoarthritis (OA).

Methods • To carry out this investigation, the researchers enrolled 65 OA patients subjects for the study. These patients were divided into 2 groups based on the severity of their OA. Thirty healthy individuals were included as the control group. All study participants underwent magnetic resonance T1rho and T2 mapping scans. OA patient scores and values from the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), T2, and a T1rho MRI measurement indicating potential early indication of bone and joint diseases from each cartilage area were compared among the OA patients as well as the control group. Pearson correlation analysis was used to examine the relationships between T2 and T1rho values and WOMAC scores.

Results • The WOMAC scores in the mild OA group were lower than the severe OA group ($P < .05$). There were no significant differences in T2 and T1rho values of lateral tibial cartilage among the 3 groups ($P > .05$). On the other hand, the T2 and T1rho values of medial femoral, lateral femoral, and medial tibial cartilage areas increased progressively in the control, mild OA, and severe OA groups ($P < .05$). A Pearson analysis found a positive correlation between the T2 values of medial, lateral, and medial tibial cartilages and the WOMAC scores. Similarly, the T1rho values of these cartilage areas were also positively correlated with the WOMAC scores.

Conclusion • Magnetic resonance T1rho and T2 mapping offer good evaluation value for assessing cartilage injury in middle-aged and elderly patients with knee OA. The values obtained from T1rho and T2 mapping in various areas of the cartilage show a positive correlation with WOMAC scores. (*Altern Ther Health Med.* 2024;30(10):308-313).

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INTRODUCTION

Osteoarthritis (OA) of the knee joint is a prevalent chronic arthropathy commonly affecting middle-aged and elderly individuals. It is characterized by joint pain and dysfunction. The leading causes of OA are meniscal and ligament injuries,[1,2] as well as subchondral lesions. In the early stages, anti-inflammatory and analgesic medications are typically utilized. At the same time, arthroscopic cleaning of local tissues is performed during the mid-stage, and arthroplasty is considered for surgery in the late stage.[3,4] Early detection and targeted intervention are essential for favorable patient outcomes.

Although arthroscopy is the preferred method for diagnosing OA, its invasive nature limits its widespread use. In recent years, Magnetic Resonance Imaging (MRI) of the knee has become a common diagnostic tool for knee trauma and periprosthetic knee diseases. It enables observation of cartilage morphology and repair and has gained popularity in the clinical diagnosis of OA.[5,6] While conventional MRI scanning provides clear visualization of cartilage thickness and cartilage volume at the joint and fracture of cartilage at the joint, microstructures such as the extracellular matrix of cartilage at the joint have been pathologically altered long before the injury.

In recent years, longitudinal relaxation time quantitative imaging (T1rho) and transverse relaxation time quantitative imaging (T2 mapping) have been introduced. These

sequences allow for the quantitative analysis of biochemical changes in the articular cartilage before any visible morphological changes.[7,8] However, no relevant research exists on the direct and specific relationship between imaging characteristics and cartilage damage.

In the current field of osteoarthritis research, particularly in imaging assessment, numerous unanswered questions require further investigation. While studies have been conducted on the use of T1rho and T2 mapping for osteoarthritis, there is a need for a comprehensive understanding of how these imaging indicators differ in various subtypes and their correlation with clinical manifestations. This study aims to analyze imaging data of mild osteoarthritis, severe osteoarthritis, and a control group to explore the performance differences between T1rho and T2 mapping in various osteoarthritis cases, thus filling existing gaps in the current literature. Building upon this foundation, this study aims to examine the effectiveness of MRI T1rho and T2 mapping imaging in assessing cartilage damage in middle-aged and elderly patients with osteoarthritis. The ultimate goal is to provide valuable insights into diagnosing and treating patients' conditions.

The application of MRI T1rho and T2 mapping technology in osteoarthritis imaging has attracted widespread attention. However, there is currently limited understanding of the variation of these imaging markers among different subtypes of osteoarthritis, as well as their correlation with clinical symptoms. This study aimed to investigate the performance differences between MRI T1rho and T2 mapping in patients with mild and severe osteoarthritis and establish a correlation between these imaging parameters and the patient's clinical symptoms. Specifically, the researchers focused on analyzing T1rho and T2 values in various cartilage zones to evaluate these techniques' potential advantages in capturing osteoarthritis's extent and clinical manifestations.

MATERIALS AND METHODS

General Information

The researchers selected 65 patients with OA admitted to the researchers' hospital between June 2021 and June 2023 as participants in this study. Among them, 24 were male and 41 were female. Their ages ranged from 37 to 73 years, with a mean age of 55.14±8.89. These patients' body mass index (BMI) ranged from 21~26 kg/m^2, with a mean BMI of 23.35±1.24 kg/m^2.

For comparison, the researchers also included 30 healthy individuals who underwent a physical examination in the hospital. Among them, 11 were male and 19 were female. The ages of these individuals ranged from 37 to 75 years, with a mean age of 55.14±9.53 years. Their BMI ranged from 21 to 26 kg/m^2, with a mean BMI of 23.66±1.32 kg/m^2.

The 2 groups had no significant differences regarding gender, age, and BMI ($P > .05$). The Second Affiliated Hospital Ethics Committee of Xingtai Medical College District approved the study.

To be eligible for this study, participants were required to meet the clinical diagnostic guidelines for OA.[9] Additionally, they should have experienced recurrent knee pain and a sensation of bones rubbing against each other during physical activity within the past month. X-ray results showed a narrowing of the joint space, sclerosis of the subchondral bone, and osteochondroma formation. Participants were also to be ≥ 38 weeks in age.

Individuals with a history of knee surgery, joint deformities, inability to straighten their knee completely, developmental variations in the meniscus, or incomplete clinical were excluded from the study. The control group, on the other hand, could not have any knee pain, limitation of movement, or underlying diseases.

MRI Examination Methods

The Philips Achieva 3.0T TX MRI scanner with the SENSE-Flex-M standard knee coil was used for the MRI examination.

Before the examination, the patient was instructed to lie down and rest for half an hour. Then, they were positioned supine with their left or right knee scanned. The foot was advanced, and the knee was kept straight, with the lower edge of the patella as the center of scanning—the scanning range included the femoral ankle and tibia. The examination consisted of conventional sagittal scanning, followed by T1rho and T2 mapping scans. All sequences were performed in one scan.

For T2WI (T2-weighted imaging), the parameters used were: TR (repetition time) shortest, TE (echo time) 62 ms, FOV (field of view) 140 mm, matrix 256×256, layer thickness 5 mm, layer spacing 5 mm, and excitation twice.

For T2WI, the parameters used were: TR 700 ms, TE 20 ms, FOV 140 mm, matrix size 256×256, layer thickness 5 mm, layer spacing 5 mm, and excitation twice.

For T1rho imaging, the parameters used were: TR 5.95 ms, TE 2.95 ms, FOV 140 mm, matrix size 256×256, layer thickness 4 mm, layer spacing 1mm, flip angle 50°, self-selected locking time 1 ms, with the number of samples taken at 10 ms, 20 ms, 30 ms, and 40 ms. The SPIR pressure lipo frequency was set at 759.5 Hz.

The scan produced a series of images that the MRI automatically processed to generate Tgrho pseudo-color maps. The T2 mapping sequence had a TR of 2700ms and TE values ranging from 16 ms to 128 ms in increments of 16 ms. The FOV was set to 140 mm with a matrix size of 256×256, layer thickness of 4mm, layer spacing of 1mm, and a sampling rate of 2 times. MRI post-processing generated a series of scanned images to produce Tmapping pseudo-color maps.

Image Processing and Analysis

Two experienced imaging physicians analyzed the films using a double-blind method. In cases of disagreement, they reached a consensus through discussion or sought guidance from a superior physician. The acquired images were then

uploaded to the GE ADW 4.4 workstation to generate T1rho and T2 mapping pseudo-color maps. The software selected the appropriate Region of Interest (ROI) and measured the T1rho and T2 values at specific sites, including the medial and lateral facets of the femur and tibia. The mean value was obtained from 6 measurements at each site.

Cartilage Damage Grading

The International Cartilage Repair Society Histological Scoring (ICRS)[10] standard was used to assess the degree of cartilage damage in patients with OA. Grade 0 represents a smooth articular cartilage surface in this grading system, with no morphological and signal abnormalities visible in the images. Grade I indicates morphologically normal articular cartilage but with abnormal internal signals. Grade II signifies a partially defective cartilage surface, with the defect depth being less than 50%. Grade III indicates a severe defect in the cartilage, with a defect depth of ≥50% but <100%. Finally, Grade IV represents 100% defective cartilage, with or without signal changes. The mild OA group included patients with Grade I and II damage, while the severe OA group included those with Grade III and IV damage. The control group consisted of individuals with Grade 0 cartilage.

Western Ontario and McMaster University Osteoarthritis Index Scores

The study employed WOMAC (Western Ontario and McMaster University) osteoarthritis questionnaires to assess the condition of the patients, specifically focusing on their pain, stiffness, and joint functionality.[11] The questionnaire comprised 24 items, each rated on a scale ranging from "normal to very severe," with scores ranging from 0 to 4. The higher the score, the more severe the patient's symptoms.

Statistical Processing

The researchers used the Statistical Package for the Social Sciences (SPSS) 22.0 to process the relevant data in this study. The measured data all exhibited a normal distribution, represented as (±s). To compare the differences among the 3 groups, the researchers employed one-way ANOVA. Additionally, the researchers conducted *Pearson* correlation analysis to analyze the relationship between T1rho and T2 values of the medial cartilage area of the femur, lateral cartilage area of the femur, and medial cartilage area of the tibia and the WOMAC scores. Any observed differences were considered statistically significant with $P < .05$. The researchers chose these statistical methods to ensure a comprehensive analysis of the cartilage parameters. The decision was based on the nature of the research question and the statistical requirements of the study.

RESULTS

Comparison of WOMAC Scores Between Mild OA Group, Severe OA Group and Control Group

The WOMAC scores in the OA group consisted of zero instances of grade 0, 23 instances of grade II, 12 instances of grade III, and 8 instances of grade IV. The mild OA group had 45 cases, while the severe OA group had 20 cases. The WOMAC scores for the mild OA group, severe OA group, and control group were (15.63±2.74), (39.86±4.37), and 0, respectively. The WOMAC score for the mild OA group was lower than that of the severe OA group, with a statistically significant difference ($P < .05$) shown in Figure 1.

Figure 1. Comparison of WOMAC Scores Between the Mild OA Group and the Severe OA Group

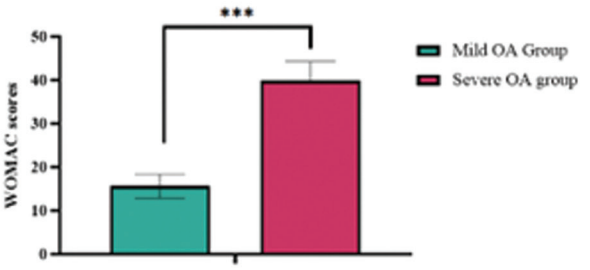
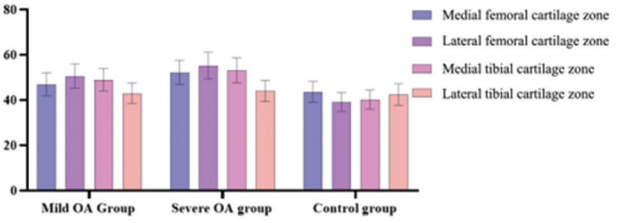


Table 1. Comparison of T1rho Values of Each Cartilage Zone in Mild OA Group, Severe OA Group, and Control Group (±s)

Group	Cases	Medial femoral cartilage zone	Lateral femoral cartilage zone	Medial tibial cartilage zone	Lateral tibial cartilage zone
Mild OA Group	45	46.92±5.08[a]	50.65±5.37[a]	48.95±4.92[a]	42.98±4.54
Severe OA group	20	52.19±5.33[a,b]	55.28±5.89[a,b]	53.14±5.50[a,b]	44.06±4.67
Control group	30	43.64±4.62	39.14±4.16	40.22±4.28	42.39±4.80
F		17.598	70.632	48.809	0.777
P value		<.001	<.001	<.001	.463

[a]compared with the control group, $P < .05$
[b]compared with the mild OA group, $P < .05$

Figure 2. Comparison of T1rho Values of Each Cartilage Zone in Mild OA Group, Severe OA Group, and Control Group



Comparison of T1rho Values in Each Cartilage Zone Between Mild OA Group, Severe OA Group, and Control Group

The comparison of T1rho values in the lateral tibial cartilage zone did not yield significant differences between the mild OA group, severe OA group, and the control group ($P > .05$). However, when comparing the T1rho values in the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone, it was observed that the control group had lower values compared to the mild OA group and severe OA group ($P < .05$). Specifically, in the medial femoral cartilage zone, the cartilage value of the mild osteoarthritis group was 46.92±5.08, for the severe OA group, was 52.19±5.33, and for the control group was 43.64±4.62. In the lateral femoral cartilage zone, the cartilage

Figure 3. Pearson Correlation Analysis

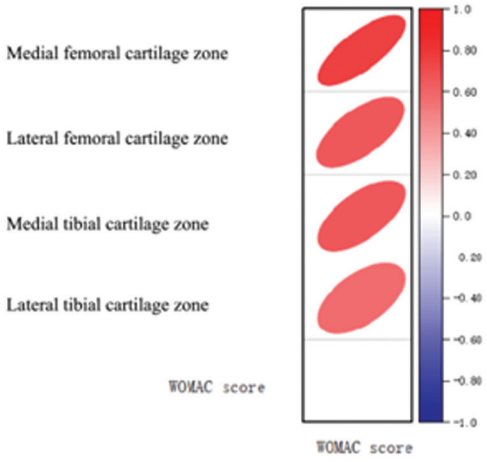
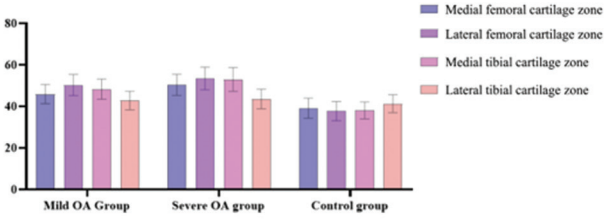


Table 2. Comparison of T2 Values of Each Cartilage Zone of Knee Joint Between Mild OA Group, Severe OA Group, and Control Group (±s)

Group	Cases	Medial femoral cartilage zone	Lateral femoral cartilage zone	Medial tibial cartilage zone	Lateral tibial cartilage zone
Mild OA Group	45	45.85±4.65[a]	50.26±5.09[a]	48.27±4.82[a]	42.83±4.50
Severe OA group	20	50.34±5.07[a,b]	53.39±5.43[a,b]	52.93±5.77[a,b]	43.50±4.76
Control group	30	39.06±4.83	37.75±4.62	38.01±4.06	41.23±4.34
F		35.859	76.595	67.023	1.802
P value		<.001	<.001	<.001	.171

[a]compared with the control group, $P < .05$
[b]compared with the mild OA group, $P < .05$.

Figure 4. Comparison of T2 Values of Each Cartilage Zone of Knee Joint Between Mild OA Group, Severe OA Group, and Control Group



value of the mild osteoarthritis group was 50.65±5.37, for the severe osteoarthritis group was 55.28±5.89, and for the control group was 39.14±4.16. In the medial tibial cartilage zone, the cartilage value of the mild osteoarthritis group was 48.95±4.92; for the severe osteoarthritis group, it was 53.14±5.50, and for the control group, it was 40.22±4.28. Lastly, in the lateral tibial cartilage zone, the cartilage value of the mild osteoarthritis group was 42.98±4.54, while the cartilage value of the severe osteoarthritis group was 44.06±4.67, and the cartilage value of the control group was 42.39±4.80. See Table 1 and Figure 2.

Relationship Between T1rho Values of Medial Femoral Cartilage Zone, Lateral Femoral Cartilage Zone, and Medial Tibial Cartilage Zone and WOMAC Score

According to the Pearson correlation analysis, there was a positive correlation between the T1rho values of the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone with the WOMAC scores (r=0.351, 0.370, and 0.384, $P < .05$) as shown in Figure 3.

Comparison of T2 Values of Each Cartilage Zone of the Knee Joint Between the Mild OA Group, the Severe OA Group, and the Control Group

The T2 values in the lateral tibial cartilage zone did not show a significant difference between the mild OA group, severe OA group, and the control group ($P > .05$). However, when comparing the T2 values in the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone, it was observed that the control group had lower values compared to the mild OA group and severe OA group ($P < .05$). Specifically, in the mild OA group, the T2 values for medial femoral, lateral femoral, and medial tibial cartilage were 45.85±4.65, 50.26±5.09, and 48.27±4.82, respectively. In the severe OA group, these values were 50.34±5.07, 53.39±5.43 and 52.93±5.77, respectively. In contrast, the control group exhibited significantly lower T2 values of 39.06±4.83, 37.75±4.62, and 38.01±4.06 for the areas mentioned above. There was no significant difference in the T2 values in the lateral tibial area among the groups. The cartilage T2 values of the mild osteoarthritis group, severe osteoarthritis group, and control group were 42.83±4.50, 43.50±4.76, and 41.23±4.34, respectively. See Table 2 and Figure 4.

Relationship Between T2 Values of Medial Femoral Cartilage Zone, Lateral Femoral Cartilage Zone, and Medial Tibial Cartilage Zone and WOMAC Score

Pearson's correlation analysis showed a positive correlation between the T2 values of the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone, and the WOMAC scores (r=0.343, 0.319, and 0.362, $P < .05$).

DISCUSSION

In recent years, the incidence of OA in the elderly has been on the rise, with cartilage injuries of the knee joint being the most common.[11] The severity of knee symptoms in OA patients is commonly evaluated using the WOMAC score, which assesses joint stiffness, pain, and functional status.[12] In the present study, it was observed that the WOMAC score was lower in the mild OA group compared to the severe OA group, indicating a significant increase in scores as OA worsened. This study analyzed the relationship between T1rho, T2 values, and WOMAC scores, providing insights into the potential application of T1rho and T2 mapping techniques for assessing the condition of OA patients.

The physiological composition of human knee cartilage primarily consists of chondrocytes and extracellular matrix, with the latter being more common. The extracellular matrix comprises a type II collagen fiber network, proteoglycan, and water, constituting the cartilage's central scaffolding. Within the cartilage, proteoglycan molecules and water are uniformly

distributed. T1rho and T2 mapping imaging are physiological MRI methods with advantages such as shorter imaging time, no need to apply contrast agents, and high image resolution. In the early stages of OA, the extracellular matrix gradually deteriorates, leading to a reduction in proteoglycan content and an increase in free water content. This results in disrupted changes in collagen fibers. T1rho and T2 mapping can detect the depletion of proteoglycans and biochemical changes in the early stages.

The present study discovered that when comparing T1rho values in different areas of the femoral and tibial cartilage, the control group had lower values than the mild OA group, and the mild OA group had lower values than the severe OA group. T1rho primarily indicates the movement between water and macromolecules at low frequencies, which reflects the content of water and macromolecules at low frequencies, which reflects the content of water and macromolecules in the cartilage. This technique has been widely utilized in previous research on cartilage diseases in the intervertebral disc, ankle joint, and wrist joint.[13]

Usually, the T1rho relaxation time is generally low when there is a high amount of proteoglycan within the cartilage tissue structure. In patients with OA, the T1rho value increases due to significant defects in the articular cartilage, leading to a decrease in proteoglycan content within the joint. The present study's findings indicate that as the severity of OA disease worsens, the T1rho values in each knee joint zone tend to increase. Pearson correlation analysis reveals a positive correlation between the T1rho values in the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone and the WOMAC score. This suggests that clinics can use these values as a reference point to assess the progression and changes in the disease.

This study successfully revealed a connection between imaging values and WOMAC scores. It is crucial to delve deeper into the practical implications of these findings for clinical practice. The correlation between imaging values and WOMAC scores can provide valuable insights for developing treatment strategies in patients with OA. For example, understanding how specific imaging parameters relate to pain, stiffness, and dysfunction can assist physicians in creating more targeted and individualized treatment plans. Different interventions may be needed to address specific abnormalities detected through imaging more effectively.

Knowledge of these correlations also holds significance for patient prognosis. By understanding the relationship between imaging findings and WOMAC scores, doctors can better predict the development of the patient's disease course and take necessary intervention measures to slow the progression of OA or alleviate symptoms. In addition, interpreting these associations can provide direction for clinical research and the development of new treatments. A deeper understanding of the link between imaging and symptoms can pave the way for advancements in medical practices.

The researchers in this study compared the T2 values of different areas of the knee joint cartilage, specifically, the medial femoral cartilage, lateral femoral area, and medial tibial area. The results showed that T2 values increased as the severity of the disease worsened, with the control group having the lowest values, followed by the mild OA group and then the severe OA group. These findings are consistent with previous studies conducted by Shi et al.[14,15]

This increase in T2 values is attributed to the T2 mapping imaging technique used in the study. This technique collects relevant data from various levels of the knee joint using a multi-echo gradient echo technique. It then produces a color scale image that represents T2 contrast. This image allows for the assessment of spin-spin interactions between adjacent protons in the knee cartilage tissues and the reflection of transverse interactions caused by phase bias due to the inhomogeneity of the magnetic field.

When the articular cartilage tissues in the bodies of OA patients become damaged, there is a significant increase in the water content of the affected cartilage. This increase in water content leads to a noticeable rise in the T2 value. Studies by Shapiro[16] and Di Matteo[17] have shown that cartilage lesions in OA patients are closely associated with mechanical damage in the surrounding tissues, which subsequently results in an elevation of cartilage T2 values.[18] Pearson's correlation analysis showed a positive correlation between the T2 values in the medial femoral cartilage zone, lateral femoral cartilage zone, and medial tibial cartilage zone and the WOMAC scores. This suggests that the T2 mapping imaging features are important in assessing OA.

Although this study offers valuable insights into the relationship between imaging values and WOMAC scores, the researchers acknowledge that the discussion lacks depth regarding future research directions. The researchers recommend that future studies focus on delving deeper into the relationship between imaging values and specific OA subtypes. Different subtypes may exhibit distinct imaging manifestations, and a deeper understanding of these differences could serve as a foundation for precision medicine advancements. By studying the imaging characteristics of specific OA subtypes, one can better understand the subtype variability of the disease, thus enabling more accurate personalized treatment approaches.

The researchers also encourage a more detailed future exploration of longitudinal changes in T1rho and T2 values. These values may change over time, and understanding these changes is critical to understanding the development of OA and changes in patients' conditions. Longitudinal studies can also help determine which imaging parameters might serve as biomarkers for early prediction of OA progression. Overall, the suggestions for future research directions will facilitate the advancement of OA management strategies and provide more robust support for clinical practice.

In conclusion, using MRI T1rho and T2 mapping techniques demonstrates significantly high clinical value for quantitative assessment of cartilage damage in OA patients. Moreover, a positive correlation exists between the T1rho and T2 values of cartilage in different parts of the knee joint

and the WOMAC score. This study provides valuable insights into the practical application of T1rho and T2 mapping in osteoarthritis, which can serve as a basis for further refining the diagnosis and treatment strategies for this condition. The researchers eagerly anticipate future research endeavors that delve deeper into the potential of these imaging tools in making more targeted contributions to improving patient care and optimizing treatment options.

ETHICAL COMPLIANCE

The ethics committee of The Second Affiliated Hospital of Xingtai Medical College District approved this study.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

LT, YGao, and CD designed the study and performed the experiments, CD and YGong collected the data, LT, YGao and YGong analyzed the data, LT, YGao and CD prepared the manuscript. All authors read and approved the final manuscript. LT and YG contributed equally to this work.

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REFERENCES

1. Hawker GA, King LK. The burden of osteoarthritis in older adults. *Clin Geriatr Med*. 2022;38(2):181-192. doi:10.1016/j.cger.2021.11.005
2. Yuan T, Cai D, Hu B, Zhu Y, Qin J. Therapeutic Effects of Curcumin on Osteoarthritis and Its Protection of Chondrocytes Through the Wnt/B-Catenin Signaling Pathway. *Altern Ther Health Med*. 2022;28(5):28-37.
3. Andriacchi TP, Lang PL, Alexander EJ, Hurwitz DE. Methods for evaluating the progression of osteoarthritis. *J Rehabil Res Dev*. 2000;37(2):163-170.
4. Murray R, Winkler PW, Shaikh HS, Musahl V. High tibial osteotomy for varus deformity of the knee. *Jaaos Glob Res Rev*. 2021;5(7):e21.00141. doi:10.5435/JAAOSGlobal-D-21-00141
5. Amendola A, Panarella L. High tibial osteotomy for the treatment of unicompartmental arthritis of the knee. *Orthop Clin North Am*. 2005;36(4):497-504. doi:10.1016/j.ocl.2005.05.009
6. MacKay J, Watkins L, Kogan F. Editorial for "local patterns in two-year t1rho and t2 changes in hip cartilage are related to sex and functional data: a prospective evaluation on hip osteoarthritis participants". *J Magn Reson Imaging*. 2023;57(4):1054-1055. doi:10.1002/jmri.28446
7. Ikuta F, Takahashi K, Kiuchi S, et al. Effects of repeated intra-articular hyaluronic acid on cartilage degeneration evaluated by T1ρ mapping in knee osteoarthritis. *Mod Rheumatol*. 2021;31(4):912-918. doi:10.1080/14397595.2020.1830483
8. Xing D, Wang Q, Chen YL, Lin JH. [Exploration on developing the diagnosis and treatment guidelines for osteoarthritis in primary care of China] [In Chinese]. *Zhonghua Wai Ke Za Zhi*. 2019;57(1):39-43.
9. García-Coronado JM, Martínez-Olvera L, Elizondo-Omaña RE, et al. Effect of collagen supplementation on osteoarthritis symptoms: a meta-analysis of randomized placebo-controlled trials. *Int Orthop*. 2019;43(3):531-538. doi:10.1007/s00264-018-4211-5
10. Copsey B, Thompson JY, Vadher K, et al. Problems persist in reporting of methods and results for the WOMAC measure in hip and knee osteoarthritis trials. *Qual Life Res*. 2019;28(2):335-343. doi:10.1007/s11136-018-1978-1
11. Jiang J, Feng S, Li Z, et al. The Expression of MDM2 Gene Promoted Chondrocyte Proliferation in Rats with Osteoarthritis via the Wnt/β-Catenin Pathway. *Cell Mol Biol (Noisy-le-grand)*. 2022;67(6):236-241. doi:10.14715/cmb/2021.67.6.31
12. Kester BS, Carpenter PM, Yu HJ, et al. T1ρ/T2 mapping and histopathology of degenerative cartilage in advanced knee osteoarthritis. *World J Orthop*. 2017;8(4):350-356. doi:10.5312/wjo.v8.i4.350
13. Shi L, Wang K, Yu J, et al. Relationship between magnetic resonance T2-mapping and matrix metalloproteinase 1,3 in knee osteoarthritis. *Indian J Orthop*. 2020;55(4):974-982. doi:10.1007/s43465-020-00293-2
14. Goto H, Iwama Y, Fujii M, et al. The natural degeneration course in the T1rho values of normal knee cartilage. *Kobe J Med Sci*. 2012;57(4):E155-E170.
15. Shapiro SA, Arthurs JR, Heckman MG, et al. Quantitative T2 MRI mapping and 12-month follow-up in a randomized, blinded, placebo controlled trial of bone marrow aspiration and concentration for osteoarthritis of the knees. *Cartilage*. 2019;10(4):432-443. doi:10.1177/1947603518796142
16. Di Matteo B, Vandenbulcke F, Kon E. Comment Regarding Article: "Quantitative T2 MRI mapping and 12-month follow-up in a randomized, blinded, placebo controlled trial of bone marrow aspiration and concentration for osteoarthritis of the knees". *Cartilage*. 2019;10(4):504-505. doi:10.1177/1947603519852400
17. Lin Z, Yang Z, Wang H, Zhao M, Liang W, Lin L. Histological grade and magnetic resonance imaging quantitative t1rho/t2 mapping in osteoarthritis of the knee: a study in 20 patients. *Med Sci Monit*. 2019;25:10057-10066. doi:10.12659/MSM.918274